PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference PCA30648/HMY	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. **PCT/KR2003/001629**	International filing date *(day/month/year)* **13 AUGUST 2003 (13.08.2003)**	Priority date *(day/month/year)* 19 AUGUST 2002 (19.08.2002)

International Patent Classification (IPC) or national classification and IPC

IPC7 C07D 221/18

Applicant

HANMI PHARM. CO., LTD. et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
02 JANUARY 2004 (02.01.2004)	09 JULY 2004 (09.07.2004)

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INTERNATIONAL P[redacted]MINARY EXAMINATION REPORT

[redacted]rnational aplication No.
PCT/KR2003/001629

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[ ] the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

[ ] the claims:
pages _____, as originally filed
pages _____, as amended (together with any statment) under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

[ ] the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

[ ] the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application(under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide** and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained inthe international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disc losure in the international applicationas as filed has been furinshed.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages _____

[ ] the claims, Nos. _____

[ ] the drawings, sheet _____

5.

[ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 6	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 6	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 - 6	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents have been considered for the purpose of this report:

D1: WO 02/46207 A2 (13 Jun. 2002)
D2: US 5804576 A (8 Sep. 1998)
D3: J. Pharm. Sci. Vol.63(1), pp.19-23 (Jan. 1974)

1. Novelty and Inventive Step

Claims 1-6 of the present invention are related to a method for preparing the 3-oxo-4-aza-5α-androstane compound of formula (I) comprising heating the 3-oxo-4-aza-5-androstene compound of formula (III) for 4-8 hrs at 80 - 130℃ in a mixture of formic acid and an alkanediol such as ethylene glycol, propylene glycol, 1,2-butanediol etc. in the presence of zinc.

D1 discloses a process for preparing a 3-oxo-4-azasteroid by hydrogenating a 4-aza-androsten-3-one in the presence of an ammonium formate and a catalyst such as Pt2O, Pd/C, and Ni at 50 - 70℃.
D2 discloses that treatment of the 7-α-hydroperoxy-3β-hydroxyandrost-5-en-17-one with zinc and acetic acid yields 3β,7α-dihydroxy-androst-5-en-17-one.
D3 discloses a process for preparing a 4-aza-5α-cholestan-3-one by hydrogenating a 4-aza-5-cholesten-3-one with N-methylformamide and formic acid at 170-185℃.

Although D1-D3 are related to methods for preparing steroids by hydrogenating the corresponding steroid alkenes, D1 and the present invention differ from each other in both the hydrogenating agents and the catalysts, and they are not easily exchangeable by those who are skilled in the art.
D2 differs from the present invention in the backbone structure of the steroid compounds and in using acetic acid, instead of a formic acid and an alkandiol. Thus, D2 cannot lead those who are skilled in the art to expect the present invention.
D3 differs from the present invention in not using zinc and using a N-methylformamide, instead of alkanediols. In addition, the reaction temperature of D3 is very harsh(170-185℃),
(Continued on Supplemental Box)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

Box V.

compared with the relatively mild temperature condition of the present invention.
Thus, those who are skilled in the art would not be able to expect the present invention from D3.

Therefore, Claims 1-6 of the present invention are considered to be novel and to involve an inventive step over D1-D3 (Article 33(2) and (3) PCT).

2. Industrial Applicability
Claims 1-6 of the present invention are considered to be industrially applicable (Article 33(4) PCT).